UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,011	01/29/2004	Masataka Andoh	Q79665	2008

23373   7590   08/28/2006

SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER
SKOWRONEK, KARLHEINZ R

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on <u>13 July 2006</u>.

2a)☐ This action is **FINAL**.   2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) <u>1-18</u> is/are pending in the application.

    4a) Of the above claim(s) <u>9-16</u> is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) <u>1-8, 17 and 18</u> is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

    a)☐ All   b)☐ Some *   c)☐ None of:

      1.☐ Certified copies of the priority documents have been received.

      2.☐ Certified copies of the priority documents have been received in Application No. _____.

      3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

    * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
    Paper No(s)/Mail Date <u>8/12/2004</u>.

4) ☐ Interview Summary (PTO-413)
    Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the invention of group I, drawn to claims

1-8 and 17-18, in the reply filed on 31 July 2006 is acknowledged.

Claim Status

Claims 1-18 are pending.

Claims 9-16 are withdrawn from further consideration pursuant to 37 CFR

1.142(b) as being drawn to a nonelected invention, there being no allowable generic or

linking claim. Election was made **without** traverse in the reply filed on 31 July 2006.

Claims 1-8 and 17-18 are being examined.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 12 Aug 2004 was filed

after the mailing date of the application on 29 Jan 2004. The submission is in

compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure

statement has been considered by the examiner.

Objections to Specification

The disclosure is objected to because of the following informalities: Spelling error

in paragraph [004] "Then, these cDAN's are...".

Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly
claiming the subject matter which the applicant regards as his invention.

1.   Claims 1-8 and 17-18 are rejected under 35 U.S.C. 112, second paragraph, as

being indefinite for failing to particularly point out and distinctly claim the subject matter

which applicant regards as the invention.

In the instant case, claims 1 and 17-18, the recitation phrase "average 0" is

vague and indefinite. It is unclear how this should be interpreted in light of the rest of the

claims and specification. Claims 2-8 are also rejected because they depend from claim

1, and thus contain the above issues due to said dependence.

Claims 1, 6, and 17-18 incorporate the use of the variable "u" which is vague. It is

unclear how "u" is to be interpreted. The specification defines "U" as the addition of the

gene expression level from channel 1 to the gene expression level from channel 2, but

does not define "u".

Claim 1 recitation of the variable "$(\mu_0, \sigma_1{}^2)$" is vague. It is unclear how this should

be interpreted.

Claim 3 recites the variable, greek letter Nu, "ν" which is vague. It is unclear how

the variable Nu should be interpreted.

Claim 5 defines the variable "g_{01} represents a mixing ratio" which is indefinite. It

is unclear what "g_{01}" represents because in the specification "g_{01}" defined as a

simultaneous distribution and the in the claims as a mixing ratio.

Claim 5 recites the equations 31, 32, 43, and 44 which is vague because said equations are matrices.

Claims 5 and 6 incorporate the use of the variable "v" which is vague. It is unclear how "v" is to be interpreted. The specification defines "V" as the difference between the gene expression level from channel 1 and the gene expression level from channel 2, but does not define "v".

Claims 6 and 7 recite the phrase "true gene expression" which is vague. It is unclear how "true gene expression" should be interpreted.

Claim 5 recite the variables (u_i, v_i). There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 17 and 18 rejected under 35 U.S.C. 102(b) as being anticipated by McLachlan et al. (The EMMIX software for the fitting of mixtures of normal and t-Components and the user's guide to EMMIX-version 1.3 1999, Journal of Statistical Software. Vol. 4(2), p. 1-14, 12 July 1999, [www.jstatsoft.org]) as evidenced by Soong (Fundamentals of probability and statistics for engineers, p.93, Wiley, 2004).

Claim 1 is directed to gene expression state estimating system for estimating the probability of gene expression in each channel, the system including an input device for sending gene expression level data, a program-controlled data analyzer, and an output device, wherein said data analyzer comprises distributed parameter estimating means for estimating distributed parameters of a mixed normal distribution shown in the following equation (25) using the gene expression level data from said input device, and sending the estimated distributed parameters: $(1-\xi)\varphi(u-\mu_0|\sigma_0^2)+ \xi\varphi(u-\mu_1|\sigma_1^2)$ (25) where $\varphi(*|\sigma^2)$ represents the density function of a one-dimensional normal distribution with average 0 and variance σ^2, $(\mu_0|\sigma_0^2)$ and $(\mu_0|\sigma_1^2)$ are average and variance parameters of first and second components, respectively, and t is the mixing ratio, with the assumption that $\mu_0 < \mu_1$, $\sigma_0^2) > 0$, $\sigma_1^2) > 0$, $0< \xi <1$ is satisfied, mixing ratio parameter estimating means for estimating a mixing ratio parameter of the mixed normal distribution using the gene expression level data sent from said input device and the distributed parameters sent from said distributed parameter estimating means, and sending the estimated mixing ratio parameter, and posterior probability calculating means for calculating the posterior probability of the expression state of each gene in each channel using the gene expression level data, the estimated distributed parameters and mixing ratio parameter, and sending the calculated posterior probability to said output device.

McLachlan et al. teach a gene expression state estimating system (The system is describe in the User's Guide to EMMIX on p. 4, paragraph 1, "systems") for estimating the probability of gene expression in each channel, the system including an input device for sending gene expression level data, a program-controlled data analyzer, and an

output device, wherein said data analyzer comprises distributed parameter estimating means for estimating distributed parameters of a mixed normal distribution shown in the following equation (25) (in general form as equation 1, p. 2) using the gene expression level data from said input device, and sending the estimated distributed parameters: $(1-\xi)\varphi(u-\mu_0|\sigma_0^2)+ \xi\varphi(u-\mu_1|\sigma_1^2)$ (25) where $\varphi(*|\sigma^2)$ represents the density function of a one-dimensional normal distribution with average 0 and variance σ^2, $(\mu_0|\sigma_0^2)$ and $(\mu_0|\sigma_1^2)$ are average and variance parameters of first and second components, respectively, and t is the mixing ratio, with the assumption that $\mu_0 < \mu_1$, $\sigma_0^2) > 0$, $\sigma_1^2) > 0$, $0< \xi <1$ is satisfied (Examples, p. 10, paragraph 1), mixing ratio parameter estimating means for estimating a mixing ratio parameter of the mixed normal distribution using the gene expression level data sent from said input device and the distributed parameters sent from said distributed parameter estimating means ("mixing proportions", p. 6, paragraph 2), and sending the estimated mixing ratio parameter, and posterior probability calculating means for calculating the posterior probability of the expression state of each gene in each channel using the gene expression level data, the estimated distributed parameters and mixing ratio parameter, and sending the calculated posterior probability to said output device ("current estimate of posterior probability, p. 6, top of page; and p. 33 of the User's guide to EMMIX, first line of text). Further, variance of a vector can be written as a covariance matrix as evidenced by

> "A convenient representation of their variances and covariances
>
> is the *covariance matrix*" (Soong, T.T., Fundamentals of
>
> probability and statistics for engineers, p.93),

thus the covariance matrix of McLachlan et al. teaches the variance in the instant claim.

The equation taught by McLachlan, $f(y; \Psi) = \sum_{i=1}^{g} \pi_i c_i(y; \theta_i)$ for estimating the distributed

parameters can be expressed as equation 25 of the instant application in the case of 2

conditions. McLachlan et al. define the variable π as the mixing ratio parameter that, in

the instant case, is represented by the variable ξ. McLachlan et al. teach the mixing

ratio parameters sum to 1, thus when considering 2 conditions, the mixing ratio for each

condition can be represented by π and $(1-\pi)$. McLachlan et al. also teach that in the

case of normal mixture model, $c_1(y;\theta_1)$ can be expressed as $\phi(y;\mu_i, \Sigma_i)$ where μ and Σ

represent the mean and covariance matrix, thus the general equation can be rewritten

as $(1-\pi)\phi(y;\mu_0, \Sigma_0) + \pi\phi(y;\mu_1, \Sigma_1)$ for 2 conditions and further reduced to equation 25 of

the instant application, $(1-\xi)\varphi(u-\mu_0|\sigma_0^2) + \xi\varphi(u-\mu_1|\sigma_1^2)$.

McLachlan et al. teach the gene expression program of claim 17 (FORTRAN, p.

3, paragraph 3) and is further described by McLachlan et al. in the User's guide to

EMMIX.

McLachlan et al. teach the computer readable medium of claim 18 which was

provided by McLachlan et al. along with the description of the system and is freely

available through the publisher internet address above.

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karlheinz R. Skowronek whose telephone number is (571) 272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KRS   MICHAEL BORIN, PH.D
                            PRIMARY EXAMINER